REMARKS

Upon entry of this reply, claims 2, 6-9 and 16-19 will remain pending

Reconsideration and allowance of the application are respectfully requested.

Statement of Interview

Applicants express appreciation for the courtesies extended by Examiner Umamaheswari Ramachandran during a June 20, 2011 telephone interview with Applicants' representative Arnold Turk.

During the interview, the examiner indicated that Supervisory Patent Examiner Screeni Padmanabhan was away from the office and would not be available for at least a couple of weeks. Accordingly, the interview was conducted and arguments were presented with the examiner indicating that the examiner will discuss Applicants' response with the supervisor upon his availability.

Applicants' representative set forth arguments pertaining to deficiencies that should be apparent from a review of the prior art used in the rejection. Applicants' representative emphasized that Teng is directed to a different use than recited by Applicants, and appears to only disclose varied uses of retinoids in the background section. It was further argued that Teng would not lead one having ordinary skill in the art to use 4-[(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid (hereinafter also referred to as "Am80"). It was stressed that none of the documents used in the rejection discloses Am80, so that none of the documents teaches or suggests use of Am80.

The examiner's attention was directed to independent claim 7 and it was noted that the claim is directed to a method for promoting formation of long-term memory from short-term

memory consolidation, comprising administering to a mammal, in need of consolidation of short-term as long-term memory. Applicants' representative argued that the claim was written based upon mutually agreeable language during previous interviews, and is directed to a method for promoting formation of long-term memory from short-term memory consolidation, comprising administering to a mammal, in need of consolidation of short-term as long-term memory, and recites the administration of Am80. Arguments further presented that the documents used in the rejection do not teach or suggest treating a population as recited in Applicants' claims and/or using Am80.

The examiner appeared to agree that Applicants' claims patentably define over the prior art used in the rejection of record, but would not make a commitment regarding allowance without her supervisor, and indicated that it would be necessary to await the availability of the examiner's supervisor.

Information Disclosure Statements

Applicants express appreciation for the inclusion with the Office Action of a signed copy of the Information Disclosure Statement form, whereby the Examiner's consideration of the Information Disclosure Statement filed July 12, 2010 is of record.

Claim Of Foreign Priority

Applicants <u>once again</u> request that the Examiner confirm receipt of the certified copy of the foreign priority application in this national stage application.

Response To Maintaining Of The Restriction Requirement

Claims 6 and 17 stand withdrawn from consideration as being non-elected, and claims 2, 7-9, 16, 18 and 19 are examined based on the merits.

Applicants are permitting claims 6 and 17 to remain pending subject to possible rejoinder upon allowance of the elected subject matter.

Response To Obviousness Rejection

Claims 2, 7-9, 16, 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,965,606 to Teng et al. (hereinafter "Teng") and Goodman (PNAS, 2003, 100, 5, 2901-05) and Etchamendy (J Neuosci, 2001, Aug 21(16) p 6423-29).

In response, and as discussed with the examiner during the above-noted interview, one having ordinary skill in the art would not have combined the disclosures in the manner asserted in the rejection. Moreover, even if for the sake of argument the disclosures were combined, Applicants' claimed subject matter would not be at hand, especially when none of the documents used in the rejection of record teaches or suggests Applicants' recited method for promoting formation of long-term memory from short-term memory, comprising administering to a mammal, in need of consolidation of short-term as long-term memory, a therapeutically effective amount of a composition to promote memory consolidation of short-term memory as long-term memory, the composition comprising Am80 as an active ingredient. In fact, the prior art used in the rejection does not teach or suggest either a method for promoting formation of long-term memory from short-term memory or Am80. **Therefore, as will be expanded upon below, the rejection does not arrive at Applicants' recited population of a mammal in need of consolidation of short-term as long-term memory let alone any use of Am80.**

As discussed with the examiner during the above-noted interview and as previously argued by Applicants, Teng broadly discloses many uses for retinoic acid, but does not provide guidance for arriving at Applicants' claimed subject matter. In this regard, it is noted that Teng discloses **a long list of uses of retinoid-like compounds that extends almost the entire length of column 1 of Teng. Teng has a shotgun disclosure with respect to background information.** The shotgun disclosure in the Background Section of Teng does not provide any direction with respect Teng's Summary of the Invention, beginning at column 3.

Thus, to show the lengthy disclosure of background information in Teng, it is noted that Teng has the following disclosure therein **(relating to background information)** with only mere mention of "neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and stroke" (as bolded), as follows:

> Compounds which have retinoid-like activity are well known in the art, and are described in numerous United States and other patents and in scientific publications. It is generally known and accepted in the art that retinoid-like activity is useful for treating animals of the mammalian species, including humans, for curing or alleviating the symptoms and conditions of numerous diseases and conditions. In other words, it is generally accepted in the art that pharmaceutical compositions having a retinoid-like compound or compounds as the active ingredient are useful as regulators of cell proliferation and differentiation, and particularly as agents for treating skin-related diseases, including, actinic keratoses, arsenic keratoses, inflammatory and non-inflammatory acne, psoriasis, ichthyoses and other keratinization and hyperproliferative disorders of the skin, eczema, atopic dermatitis, Darriers disease, lichen planus, prevention and reversal of glucocorticoid damage (steroid atrophy), as a topical anti-microbial, as skin anti-pigmentation agents and to treat and reverse the effects of age and photo damage to the skin. Retinoid compounds are also useful for the prevention and treatment of cancerous and precancerous conditions, including, premalignant and malignant hyperproliferative diseases such as cancers of the breast, skin, prostate, cervix, uterus, colon, bladder, esophagus, stomach, lung, larynx, oral cavity, blood and lymphatic system, metaplasias, dysplasias, neoplasias, leukoplakias and papillomas of the mucous membranes and in the treatment of Kaposi's sarcoma. In addition, retinoid compounds can be used as agents to treat diseases of the eye, including, without limitation, proliferative vitreoretinopathy (PVR), retinal detachment, dry eye and other corneopathies, as well as in the treatment and prevention of various cardiovascular diseases, including, without limitation, diseases associated with lipid metabolism such as dyslipidemias, prevention of post-angioplasty restenosis and as an agent to increase the level of circulating tissue plasminogen activator

> (TPA). Other uses for retinoid compounds include the prevention and treatment of conditions and diseases associated with human papilloma virus (HPV), including warts and genital warts, various inflammatory diseases such as pulmonary fibrosis, ileitis, colitis and Krohn's disease, **neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and stroke**, improper pituitary function, including insufficient production of growth hormone, modulation of apoptosis, including both the induction of apoptosis and inhibition of T-cell activated apoptosis, restoration of hair growth, including combination therapies with the present compounds and other agents such as Minoxidil®, diseases associated with the immune system, including use of the present compounds as immunosuppressants and immunostimulants, modulation of organ transplant rejection and facilitation of wound healing, including modulation of chelosis.

In contrast to the long background information list discussing background information, Teng discloses in the Summary of the Invention section the treatment of tumors without having one or more undesirable side effects of retinoids, as follows:

> It has been discovered in accordance with the present invention that retinoid-like compounds which act selectively, or preferably even specifically on RAR_α receptor subtypes in preference over RAR_β and RAR_γ receptor subtypes, possess desirable pharmaceutical properties associated with retinoids, and are particularly suitable for treatment of tumors, such as acute monocytic leukemia, cervical carcinoma, myeloma, ovarian carcinomas and head and neck carcinomas, without having one or more undesirable side effects of retinoids, such as inducement of weight loss, mucocutaneous toxicity, skin irritation and teratogenecity.

Accordingly, Teng is directed to treatment of tumors without having one or more undesirable side effects of retinoids, such as inducement of weight loss, mucocutaneous toxicity, skin irritation and teratogenecity, and Teng directs his disclosure of retinoids with the aim avoiding one or more undesirable side effects of retinoids. In fact, the first full paragraph a column 10 of Teng indicates that topical application is preferred.

Teng does not provide any teaching or suggestion for arriving at a method for promoting formation of long-term memory from short-term memory, comprising administering to a mammal, in need of consolidation of short-term as long-term memory, a therapeutically effective amount of a composition to promote memory consolidation of short-term memory as long-term

memory, the composition comprising 4-[(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid as an active ingredient.

Still further, Teng broadly discloses a generic formula that may encompass Am80. However, Teng does not appear to provide explicit disclosure of Am80 and/or any direction to arrive at Am80. Accordingly, for this additional reason, Teng does not provide any teaching or suggestion for arriving at the claimed subject matter.

Expanding upon the above, Teng discloses beginning at column 7, line 41 (with bold emphasis added) discloses preferred substituents that would not lead to Applicants' recited Am80:

> Referring now to the W1 and W2 groups in Formula 1, these groups are, generally speaking, electron withdrawing groups, which are present in the compounds of the invention either in the aromatic portion of the condensed ring system, or as a substituent of the aryl or heteroaryl group Y. Preferably a **W2 group is present in the Y group**, and a **W1 group is also present in the aromatic portion of the condensed ring system**. When the Z group is S (thioamides) a W1 or W2 group does not necessarily have to be present in the compounds of the invention in accordance with Formula 1, although preferably at least one of the W1 or W2 groups is nevertheless present. **In the aryl or heteroaryl Y moiety in the compounds of Formula 1 and Formula 2 as well, the W2 group is preferably located in the position adjacent to the B group**; preferably the B group is in para position in the phenyl ring relative to the "amide" moiety, and **therefore the W2 group is preferably in meta position relative to the amide moiety**. Where there is a W1 group present in the aromatic portion of the condensed ring system of the compounds of Formula 1, it preferably occupies the 8 position of the chroman nucleus with the Z=C--NH-- group occupying the 6 position. In tetrahydronaphthalene compounds of Formula 1, the Z=C--NH-- group is preferably in the 2-position, and the W1 group is preferably in the 4 position. However, when the W1 group is OH in compounds of Formula 1, then the OH is preferably in the 3 position of the tetrahydronaphthalene ring.
>
> Preferred W1 and W2 groups are F, NO_2, Br, I, CF_3, ClN_3, and OH. **The presence of one or two fluoro substituents in the Y group (W2) is especially preferred. When the Y group is phenyl, the fluoro substituents preferably are in the ortho and ortho' positions relative to the B group, which is preferably COOH or COOR8.**

Still further, Teng discloses the compounds that are most preferred in his method of treating tumors in Tables 1 and 2, and exemplified compounds in his examples that would not lead one having ordinary skill in the art to arrive at Am80, especially in view of the preferred substituents of Teng.

With regard to the above, the examiner's attention is directed to *Takeda Chem. Indus. V. Alphapharm Pty., Ltd.,* 492 F.3d 1350, 1356 (Fed. Cir. 2007) which teaches that in order to establish a *prima facie* case for obviousness with regard to a novel compound, the motivation of one having ordinary skill in the art to conduct a chemical modification of a known compound in a particular manner is important. In *Takeda*, the Court noted that in "cases involving new chemical compounds, *it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound."* (emphasis added). Id. at 1357. Under the present circumstances, Teng does not teach or suggest Am80 let alone Applicants' recited method which includes administering Am80.

The rejection attempts to overcome the deficiencies of Teng by relying upon disclosures from Etchamendy and Goodman. However, one having ordinary skill in the art would not have combined the disclosures of these documents with Teng in view of their diverse disclosures. Moreover, even if for the sake of argument the disclosures were combined, any proper combination of the disclosures would not arrive at the claimed subject matter.

Etchamendy is directed to the alleviation of a selective age-related relational memory deficit in mice by pharmacologically induced normalization of brain retinoid signaling. In contrast, Teng is directed to treatment or prevention of malignant tumors or leukemic disease or condition. Accordingly, one having ordinary skill would not have combined the disclosure of

Etchamendy with Teng. Accordingly, the combination of Etchamendy and Teng is without appropriate basis at least for this reason.

Moreover, Etchamendy is discussed and contrasted at page 2, lines 12-15 in Applicants' originally filed application. As noted in Applicants' specification, Etchamendy may suggest suppression of reduction of already consolidated long-term memory by retinoic acid, **but does not teach or suggest any action of retinoic acid on the consolidation process of short-term to long-term memory. Moreover, Etchamendy does not teach or suggest Am80 and/or administering of Am80.** Therefore, while one having ordinary skill in the art would not have combined the disclosures of Etchamendy and Teng, even if the disclosures were combined, any proper combination would not have arrived at a method for promoting formation of long-term memory from short-term memory, comprising administering to a mammal, in need of consolidation of short-term as long-term memory, a therapeutically effective amount of a composition to promote memory consolidation of short-term memory as long-term memory, the composition comprising 4-[(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid as an active ingredient.

Still further, Goodman does not overcome the deficiencies of either Teng or Etchamendy or any combination thereof. The rejection relies upon the abstract of Goodman for its disclosure that late onset Alzheimer's disease is influenced by the availability in brain of retinoic acid, and the rejection contends that it is known in the art that memory fixation disorders are main symptoms of Alzheimer's disease. However, Goodman only discloses in the abstract that:

> These findings suggest testable experiments to determine whether increasing the availability of retinoid in brain, possibly through pharmacologic targeting of the RA receptors and the cytochrome P450 RA-inactivating enzymes, can prevent or decrease amyloid plaque formation.

Thus, Goodman does not appear to disclose a method for promoting formation of long-term memory from short-term memory, comprising administering to a mammal, in need of consolidation of short-term as long-term memory. **Moreover, Goodman discloses retinoic acid but does not disclose Am80.** In fact, Goodman discloses at page 2904, at the paragraph beginning at the end of the left-hand column, potential therapies for future testing that pertain to use of drugs that increase RA synthesis. Accordingly, Goodman does not teach or suggest using any non-natural retinoid let alone Am80.

Still further, Goodman appears to relate to preventing or decreasing amyloid plaque formation, and does provide disclosure as relied upon in the rejection. Accordingly, if this ground of rejection is maintained, the Examiner is specifically requested where Goodman teaches or suggests any disclosure relating to consolidating memory let alone consolidating short-term as long-term memory.

The only reference to any documentation relating to Am80 in the Final Office Action is Hashimoto et al. (at the bottom of page 6 of the Final Office Action). However, Hashimoto is not used in the rejection of record, and reference thereto is improper with respect to the rejection of record.

The rejection appears to be arguing inherency. However, inherency cannot be present here as inherency of Applicants' recited method must be the necessary result when performing the process recited in the prior art and not merely a possible result. In contrast, the primary reference of Teng does not disclose either Applicants' recited method and/or any desirability of treating a population in need of consolidation of short-term as long-term memory, and does not teach or suggest administration of Am80.

Accordingly, at least for the reasons set forth above, withdrawal of the rejection of record with allowance of the application is respectfully requested. If for any reason, the application is not considered to be in condition for allowance, the examiner is requested to contact the undersigned to conduct the interview with the examiner's supervisor being present.

CONCLUSION

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the restriction requirement and rejection of record, and allow each of the pending claims.

Applicants therefore respectfully request that an early indication of allowance of the application be indicated by the mailing of the Notices of Allowance and Allowability.

Should the Examiner have any questions regarding this application, the Examiner is invited to contact the undersigned at the below-listed telephone number.

Respectfully Submitted,
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